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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/768,840	HILLMAN ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2003 and 24 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 21-26* is/are pending in the application.

4a) Of the above claim(s) *1,13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-12 and 21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed August 19, 2003 is acknowledged and has been entered.

2. The amendment filed October 24, 2003 is acknowledged and has been entered. Claims 21-23 have been amended.

3. The declaration under 37 CFR § 1.132 by Michael Furness filed October 24, 2003 is acknowledged and has been entered.

4. Claims 1-14 and 21-26 are pending in the application. Claims 1, 13, and 14 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 5.

5. Claims 2-12 and 21-26, insofar as the claims are drawn to the elected species of invention, are currently under prosecution.

Election/Restrictions

6. At page 18 of the amendment filed October 24, 2003, Applicant's have stated there is a presumption that the method claims will be rejoined upon determining allowability of the product claims from which they depend.

In reply, where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance,

whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Priority

7. In view of the amendment and upon consideration of Applicant's remarks, this application is given the benefit of the earlier filing dates of US Application Nos. 09/206,499 and 08/828,242.

Grounds of Objection and Rejection Withdrawn

8. Unless specifically reiterated below, the grounds of objection and rejection set forth in the previous Office action mailed July 24, 2003 have been withdrawn.

Response to the Declaration under 37 CFR § 1.132

9. The merit of the declaration under 37 CFR § 1.132 by Michael Furness has been carefully considered but not found sufficient to overcome the rejections of the claims under 35 USC §§ 101 and 112, first paragraph set forth in the previous Office action. The reasons the declaration has not been found sufficient are set forth below.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 2-12 and 21-26 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth in the previous Office action mailed July 24, 2003.

Applicant has traversed this ground of rejection providing the declaration under 37 CFR § 1.132 by Michael Furness and arguing the person of ordinary skill would have routinely and readily appreciated that the disclosed invention has specific and substantial utility. The declaration states and Applicant has asserted the usefulness of the polypeptide of SEQ ID NO: 1 as a research tool in a number of gene and protein expression monitoring applications, which were well known at the time to be useful in connection with development of drugs and monitoring the activity of such drugs, fulfills the requirements set forth under 35 USC § 101. Applicant has therefore asserted the rejection is improper and argued the use of polypeptides expressed by humans as tools for toxicology testing, drug discovery, and the diagnosis of disease is now well established. In addition, Applicant has argued, membership of the polypeptide bound by the claimed antibody in the calcium-binding protein family demonstrates utility.

The declaration refers to numerous publications and/or attachments; although the declaration states copies of these publications and/or attachments are provided,

none have been received. Therefore, the publications to which the declaration refers have not been considered, but the statements set forth in reference to these publications have been.

A copy of the email from the Dr. Cynthia Afshari to an Incyte employee to which Applicant refers has not been provided and has not been considered.

Applicant has argued the claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease. However, in each instance, given only the benefit of the existing disclosure of the invention, the claimed antibodies, the polypeptides to which the claimed antibodies bind, or the nucleic acid molecules encoding the polypeptides to which the claimed antibodies bind cannot be regarded as having immediate, practical, and beneficial utility in the "real-world".

Regarding the asserted usefulness of the claimed invention in diagnosing disease, without knowledge of which disease might be diagnosed using the claimed invention, one skilled in the art could not know how to use the invention. An actual relationship between the expression and activity of the protein to which the claimed antibody binds, or the polynucleotide encoding the protein, and any particular disease is not disclosed in the specification. Accordingly, given only the benefit of the present disclosure, it would be not be now be *practical* to use the invention, as disclosed, to diagnose a disease. Therefore, the specification is merely an invitation to the skilled artisan to determine if there is an actual relationship between the expression and activity of the protein to which the claimed antibody binds and any particular disease, and then to determine if the claimed invention can be used to diagnose such a disease.

Similarly, it would not now be practical to perform toxicology testing or to screen for drugs, because the specification does not specify the basis upon which a drug should be selected. The specification paradoxically contemplates both an agonist and an antagonist of the activity of the polypeptide for use as a therapeutic agent, and without providing any guidance or direction as to which might be better suited for use in treating a particular disease or disorder. Since generally the purpose of drug screening is to identify a drug that has a particular effect, it is unclear how one might benefit from using the claimed invention to screen drugs, since one could not know what effect

should be sought given only the benefit of the Applicant's instant disclosure. Therefore, only given benefit of the existing disclosure of the invention, the claimed invention cannot be regarded as practically useful in "real-world" drug screening.

Moreover, the assertion that the claimed antibodies, the polypeptides to which the claimed antibodies bind, or the nucleic acid molecules encoding the polypeptides to which the claimed antibodies bind can be used in an abstract capacity to screen drugs lacks the necessary substantiality of an asserted utility in the chemical arts that might otherwise fulfill the requirements of 35 USC § 101, because any benefit that might be derived by the public for a grant of a patent monopoly of the existing information disclosed by Applicant's application could not be derived immediately and directly therefrom or without need to first complete the inventive process by performing additional experimentation to characterize the functional significance of the polynucleotide sequence in the pathology or etiology of a disease, or in the pharmacology of a particular drug. To fulfill the requirements of 35 USC § 101, the skilled artisan must be able to use a claimed invention in the manner asserted by Applicant to provide some immediate benefit to the public. See *Nelson v. Bowler and Crossley*, 206 USPQ 881 (CCPA, 1980).

Furthermore, Applicant has argued the polynucleotide sequence encoding the protein to which the claimed antibody binds can be used as a probe in chip bases technologies to monitor gene expression. The Examiner does not dispute that the polynucleotide sequence encoding the protein to which the claimed antibody binds can be used as a probe in chip bases technologies to monitor gene expression. In fact, does not dispute the generic usefulness of any nucleic acid molecule as a probe, nor does the Examiner dispute the generic usefulness of any such probe in applications designed to monitor the expression of, or detect a gene encoding the polynucleotide sequence of which the probe is composed, e.g., Northern blot analysis, Southern blot analysis, cDNA microarray analysis. However, because a nucleic acid molecule is generically useful as a probe, the assertion that the polynucleotide encoding the protein to which the claimed antibody binds can be used as a probe lacks specificity, because any benefit that might be derived by the public for a grant of a patent monopoly of the

existing information disclosed by Applicant's application is not specific to the substance and nature of the polynucleotide encoding the protein to which the claimed antibody binds. See *Brenner, Comr Pats v. Manson*, 148 USPQ 689 (US SupCt, 1966).

Furthermore, it is duly noted a microarray comprising the polynucleotide encoding the protein to which the claimed antibody binds is no more, and no less useful than a probe comprising the polynucleotide sequence encoding the protein to which the claimed antibody binds; however, because specific knowledge of the biological or functional significance of the polynucleotide or protein encoded thereby is not disclosed in the specification, the existing information that would be imparted to the artisan should a patent monopoly be granted upon the application would not be sufficient to enable the artisan to use the claimed invention in the manner asserted, so as to provide an instant and specific benefit to the public. Moreover, in the absence of knowledge of the biological or functional significance of the polynucleotide or protein encoded thereby, e.g., the established association of its level of expression with the onset of cancer, the asserted use of the polynucleotide as a probe in a microarray to monitor gene expression is a general utility attributed to the broad class of the invention, not a specific utility attributed to its unique nature and substance or novelty.

For the same reasons, although Applicant has argued the protein to which the claimed antibody binds can be used as part of an array or 2-D PAGE map to monitor protein expression, because the protein or the antibody is generically useful as a probe, any benefit that might be derived by the public for a grant of a patent monopoly of the existing information disclosed by Applicant's application is not specific to the substance and nature of the protein to which the antibody binds.

As to Applicant's argument the claimed antibodies, the polypeptides to which the claimed antibodies bind, or the nucleic acid molecules encoding the polypeptides to which the claimed antibodies bind can be used monitor the activities of drugs, it is unclear how the public might hope to immediately derive benefit from practicing such an assay. Granted, given the benefit of existing disclosure, the artisan could determine if, for example, exposing tumor cells to doxorubicin affects the expression of the gene encoding the protein to which the claimed antibody binds; in doing so, the artisan could

certainly gain some information about a potential cancer drug candidate or potential toxin, namely information as to whether or not the substance affects the expression of the gene. However, given only the existing disclosure, the skilled artisan would not think such a use for the claimed invention practical, because there is simply no sound scientific rationale disclosed in the specification upon which to even propose that such an assay be performed. The benefit that might be derived by the public in doing so is proverbially tantamount to that which might be gained by "a shot in the dark" without any knowledge of what target might lie in the dark. The reason being that the specification does not disclose which, if any disease or disorder might be associated with the expression of the gene, or which, if any pharmocologic agents used to treat such diseases or disorders might act by affecting the expression of the gene. Again, even given the existing disclosure, one skilled in the art could not know specifically how the protein to which the claimed antibody binds, or the polynucleotide sequence encoding the protein, could be used in an assay that monitors the effects of drugs upon the expression of the gene as a means to evaluate the efficacy or toxicology of select drugs, because the skilled artisan would not have any sound rationale for selecting the drugs to be evaluated. Therefore, it is not apparent how the inclusion of the polynucleotide encoding the protein to which the antibody binds in a cDNA microarray, for example, could provide the public with any immediate and specific benefit. Again, the pertinent question is not whether or not the polynucleotide can be used in the manner asserted, but whether the use of the claimed invention in the manner asserted will provide the public with any immediate and specific benefit.

Moreover, in the absence of specific knowledge of the biologic or functional significance of the protein to which the claimed antibody binds, the assertion that the polynucleotide encoding the protein be used to construct a microarray for use in monitoring gene expression merely constitutes an invitation to the artisan to complete the inventive process, or rather to elaborate a "real-world" use for the polynucleotide by conducting investigations aimed at understanding the biologic or functional significance of the protein to which the claimed antibody binds, or the gene encoding the protein. As an example, through additional investigation, one might discover the gene encoding the

protein to which the claimed antibody binds is over-expressed in tumor cells compared to normal, healthy cells, in which case the artisan might develop a diagnostic assay that differentiates tumor cells from normal, healthy cells. On the other hand, one might discover the gene is not expressed in a dysfunctional immune cell and then discover that enforced expression of the gene restores the cell's normal function, in which case the artisan would have a sound rationale to screen a library of agents to identify an agent that restores the expression of the gene. However, in either case, the existing information disclosed by Applicant's application would merely provide the artisan with an invitation to perform such investigations, which might ultimately lead to a derivation of a specific benefit, or which might not; and in either case, an immediate benefit could not be derived from the use of the claimed invention because the existing information is insufficient to enable the artisan to use the claimed invention in the manner asserted to provide an immediate benefit. Although the disclosure of the claimed invention might tomorrow command the grateful attention of the public, the Court has decided:

> [A] patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.

Brenner, Comr. Pats. v. Manson, 148 U.S.P.Q. 689 at 696 (US SupCt, 1966).

Applicant has argued membership of the protein to which the claimed antibody binds in a family of calcium-binding proteins establishes the utility of the claimed invention. However, the issue at hand is whether or not the specification asserts that the claimed invention has a practical, "real-world" utility that is specific to the substance and nature of the claimed invention, the use of which, as the invention is currently disclosed, would provide an immediate benefit to the public. The public would not immediately benefit from the disclosure that the protein of SEQ ID NO: 1 more probably than not binds calcium, because the protein cannot now be used in any practical manner. The actual biologic function of the protein is not simply to bind calcium; and the actual biological function of the protein is not presently known or disclosed in the specification. Because the class of proteins, which share the common property of binding calcium, have highly variant functions, the skilled artisan cannot use the claimed invention without having to first study the function of the protein and then to elaborate a

use for the protein based upon the discovery made during the study. It were deemed practical to use the claimed invention without certain knowledge of the activity of the protein to which the claimed antibody binds, but *arguendo*, considering the widely variant roles that members of the class of proteins that bind calcium have in cell processes, the claimed invention could not be used with any degree of particularity without knowledge of precisely how the claimed invention functions. For example, the expression and activity of calcium-binding proteins, as a broad class of proteins, are not etiologically or causatively associated with cancer or immune disorders, although some members of the family are, most are not. While perhaps the claimed invention will eventually prove useful in diagnosing disease, the existing disclosure of the invention would not enable the artisan to now use the invention to diagnose a disease, because the specification does not teach which, if any disease can be diagnosed using the polynucleotide encoding the protein to which the claimed antibody binds as a diagnostic marker. Even given the disclosure of the invention, how could the artisan know how the claimed invention could be used as a practical means of diagnosing a disease in a manner specifically attributable to the particular nature and substance of the protein to which the claimed antibody binds, or of the gene encoding the protein? The answer: one could not without first investigating how the claimed invention can be used. Accordingly, the asserted utility of the claimed invention in diagnosing a disease or disorder could not provide the public with an immediate benefit, and therefore the claims are not supported by a specific and substantial asserted utility. Therefore, contrary to Applicant's assertions, membership in a class of proteins is not proof of the member's utility.

Applicant has argued all genes and the proteins encoded thereby have are useful in toxicological screening and thus all genes and the proteins encoded thereby have a well-established utility. A "well-established" utility is a specific, substantial, and credible utility, which is readily apparent, or implied by the disclosure of the properties of a material, alone or taken with the knowledge of the skilled artisan. Applicant's remark affirms the fact that the asserted utility of the polynucleotide or polypeptide in toxicological screening is generic, or lacks specificity that is readily apparent or implied

by the disclosure of the particular properties of the protein to which the claimed antibody binds, rather than by art recognized, general properties of the class of compound.

Applicant has argued that no expressed gene is irrelevant to screening for toxicological effects, since some genes, the expression of which is not affected by toxicological compounds, can be used as controls. While appreciating the possible utility of the polynucleotide encoding the protein to which the claimed antibody binds to monitor the expression of a control gene, the expression of which might be found to remain constant across a large set of array experiments, the artisan's use of the claimed invention in this manner cannot produce an immediate benefit to the public, because the existing disclosure of the invention does not teach whether the expression of the gene encoding the protein to which the claimed antibody binds is generally unaffected by toxicological compounds, nor does the disclosure teach which particular toxicological compounds do or do not affect the expression of the gene. In each set of array experiments designed to study the effect of a particular toxicological compound, it will be necessary to first determine if the gene encoding the protein to which the claimed antibody binds is useful in the assay, and if so, how the gene might be useful. Therefore, the artisan's use of the claimed invention in the manner asserted could not provide any immediate and specific benefit to the public, since the existing disclosure of the invention would not teach the artisan how the invention can be used in toxicological screening and further investigation would be required before the invention could be used with any reasonable degree of practicality. Accordingly, the usefulness of the claimed invention in the manner asserted is not a "well-established" utility since its use would not be enabled, i.e., readily apparent or implied, by the disclosure of the particular properties of the protein to which the claimed antibody binds or the polynucleotide encoding the protein.

Applicant has suggested that the antibody, the protein to which the antibody binds, and the polynucleotide encoding the protein to which the antibody binds are tools, rather than objects of research, and are therefore immediately useful. Granted the claimed invention might now be used as a tool in a general application, but before the claimed invention can be used as a tool in a specific application, it must first be used

as an object of research, since for the reasons already discussed, only further investigation can determine if, and how the polynucleotide sequence can be used in a specific manner as a tool, and in what context.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 2-12 and 21-26 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention for the reasons set forth in the previous Office action mailed July 24, 2003.

14. Claims 2-12, 21-23, and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the previous Office action mailed July 24, 2003.

Applicant has traversed this ground of rejection arguing the specification provides an adequate written description of the claimed antibodies, which specifically bind to the recited "variants" of SEQ ID NO: 1, because the present claims specifically define the claimed genus through recitation of chemical structure and because the genus is not "highly variant". In addition, Applicant has argued the state of the art at the time the application was filed was further advanced than at the time of the Lilly and Fiers applications.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The claims are drawn to a genus of antibodies, which bind to a genus of naturally occurring proteins, which are merely described as having 80% identity to the amino acid sequence of SEQ ID NO: 1 and having the ability to bind calcium. The specification teaches the members of the genus of proteins having the ability to bind calcium retain a common structural motif, namely the E-F hand motif, which is a small domain consisting of two alpha helices separated by a loop of 12 to 13 amino acid residues. The specification discloses the genus of proteins having such a motif is highly variant group of proteins, as the proteins have highly different structures and functions. The claims are drawn to antibodies, which bind naturally occurring members of the genus of proteins, which have yet to be discovered or described, either in terms of their structures or functions. The presence of the E-F hand motif does not provide an indication of the function of the protein; it merely suggests the protein may bind calcium.

Therefore, the specification does not disclose distinguishing and identifying features of a representative number of members of the genus of polypeptides to which the claims are drawn, such as a correlation between the structure of the polypeptide of SEQ ID NO: 1 and its recited function, so that the skilled artisan could immediately

envision, or recognize at least a substantial number of members of the claimed genus of compositions. Moreover, the specification fails to disclose which amino acid residues are essential to the function of the polypeptide of SEQ ID NO: 1, or which amino acids might be replaced or deleted so that the resultant polypeptide retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant polypeptide retains the activity of its parent. Accordingly the structures of the proteins to which the claimed antibodies bind cannot be predicted, particularly since the proteins are naturally occurring. Therefore, the specification fails to adequately describe at least a substantial number of members of the claimed genus of compositions comprising polypeptides that are naturally occurring variants of the polypeptide of SEQ ID NO: 1.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106). As evidenced by the teachings of numerous references cited in the previous Office action, the art is unpredictable. Therefore, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 2, 4, 5-9, and 22-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4 and 5 of US Patent No. 6,194,385 B1 for the reasons set forth in the previous Office action mailed July 24, 2003.

At Applicant's request, this issue is held in abeyance until such time that there is an indication of allowable subject matter.

Conclusion

17. No claims are allowed.

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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